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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/713,889	11/14/2003	Benjamin Levinson	WELLSP 3.0-003	1106
48394	7590	04/14/2006	EXAMINER	
DIEHL SERVILLA LLC 77 BRANT AVE SUITE 110 CLARK, NJ 07066			KRISHNAN, GANAPATHY	
			ART UNIT	PAPER NUMBER
			1623	
DATE MAILED: 04/14/2006				

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/713,889	Applicant(s) LEVINSON ET AL.	
	Examiner Ganapathy Krishnan	Art Unit 1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 January 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 2-5, 8-31 and 34-37 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 2-5, 8-31 and 34-37 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The Request for Continued Examination filed 1/30/2006 has been received, entered and carefully considered. The following information provided in the amendment affects the instant application:

1. Claims 1, 6-7 and 32-33 have been canceled.
2. Claims 2, 5, 11, 34 and 36-37 have been amended.
3. Remarks drawn to claim objections and rejections under 35 USC 112, second paragraph and 103.

Claims 2-5, 8-31 and 34-37 are pending in the case.

The text of those sections of Title 35, U. S. Code not included in this action can be found in a prior Office action.

Claim Objections

The objection to claim 2 has been overcome by amendment. The following objections are made of record.

Claim 2 is objected to because of the following informalities: The term “mesoporphyrin” has been misspelled as “mesoporhyrin”. Appropriate correction is required in this and any other claims wherein the said term is misspelled.

Claim 21 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 21 is drawn to the method of claim 11 but recites process

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steps for making the tin mesoporphyrin of claim 11. This recitation is not seen to further limit the parent claim.

Claim 23 is objected to because of the following informalities: The terms “catalyst for” should be replaced by the recitation, “catalyst to”.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The rejection of claims 1-4, 6-31 and 33-37 advanced in the previous office actions have been overcome by amendment and applicants’ arguments. The following rejections are made of record.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1-5 and 8-31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant’s amendment filed 1/30/2006 with respect to claims 1-5 and 8-31 has been fully considered but is deemed to insert new matter into the claims since the specification as originally filed does not provide support for the negative limitations, “wherein the tin mesoporphyrin is not derivatized with a complexing agent”. Nowhere can the negative

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limitations be found in the specification. Even though applicants point out to the specification, paragraphs 0043-0060, which give examples of complexes formed with tin mesoporphyrin and amino acids, the terms “complexing agent” has not been defined in the specification.

Any negative limitation or exclusionary proviso must have basis in the original disclosure. See *Ex parte Grasselli*, 231 USPQ 393 (Bd. App. 1983), *aff'd mem.*, 738 F.2d 453 (Fed. Cir. 1984). The mere absence of a positive recitation is not basis for an exclusion. Any claim containing a negative limitation, which does not have basis in the original disclosure, should be rejected under 35 U.S.C. 112, first paragraph as failing to comply with the written description requirement. See MPEP § 2163 - § 2163.07(b) for a discussion of the written description requirement of 35 U.S.C. 112, first paragraph.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5 and 8-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 has been amended to recite complexing agent. Since the mesoporphyrin is acting as a complexing agent, it is not clear if the term complexing agent is intended to mean a second agent that is different from the mesoporphyrin.

Claim 23 recites, “subjecting a reaction mixture of hemin and hydrogenation catalyst to a first elevated temperature and a first period of time”. It is not clear what applicants intend. Do applicants mean subjecting a mixture of hemin and a catalyst in the presence of hydrogen to a

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first elevated temperature? The claim has to be reworded clearly convey what is intended. The term "elevated" in claim 23 is a relative term that renders the claim indefinite. The term "elevated" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. A specific temperature or a temperature range has to be recited in this and any other claim wherein the said term is recited.

Claim 26 recites the limitation "hydrogen pressure" in claim 25, which goes back to claim 23. There is insufficient antecedent basis for this limitation in the claim. It is not clear from the recitation of parent claim 23 that the method involves hydrogenation, even though the parent claim recites hydrogenation catalyst. Clarification is needed.

Claims that depend from a rejected base claim that is unclear/indefinite are also rendered unclear/indefinite and are rejected for the same reasons.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 22, 29 and 30 are rejected under 35 U.S.C. 102(b) as being anticipated by Kappas et al (US 4,692,440).

Kappas et al teach a pharmaceutical composition comprising tin mesoporphyrin (SnMP) in aqueous sodium chloride (col. 4, lines 26-35; col. 3, line 45 through col. 4, line 8). This

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constitutes a pharmaceutical composition including a metal mesoporphyrin compound, wherein the metal mesoporphyrin compound is mesoporphyrin dichloride, as instantly claimed.

The process by which the metal mesoporphyrin compound is made, as recited in instant claim 29 is not given patentable weight.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 2-5, 8-10, 22, 29-31 and 34-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Robinson (US Patent Pub. No. 2003/0100752) in combination with Drummond (Annals of New York Academy of Sciences, 1987, 514, 87-95) and Bettelheim et al (General, Organic and Biochemistry, 1998, page 596).

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

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claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Robinson teaches tin mesoporphyrin complexed with amino acid (page 45, claim 1), wherein the substitutions R1-R12 can be H, alkyl or alkenyl and could also be substituents that carry amino acid residues (page 46, left column, middle; page 34, left column, paragraph 200). One of the preferred metal ions complexed to the core is Tin (page 32, paragraph 183). Formulations comprising the porphyrins of Robinson's invention can be optimized to contain between 0.1 and 50 mg (page 33, paragraph 193). The compounds of Robinson can be applied as aqueous solutions (page 35, paragraph 211). This means that the tin-mesoporphyrins of Robinson's invention are water-soluble.

Robinson teaches a method of treating psoriasis using the water-soluble mesoporphyrin compounds complexed with amino acid (page 35, paragraph 211).

Drummond, drawn to metalloporphyrins, teaches control of heme metabolism using tin-protoporphyrins (page 87, introduction, last paragraph). Tin protoporphyrin was by far the most potent (page 88, Results and Discussion; page 89). Tin protoporphyrin is structurally similar to tin-mesoporphyrin except that the protoporphyrin has an ethylene side chain. In the mesoporphyrin, the ethylene side chain is saturated. According to Robinson (above), the side chain can be an alkenyl. When it is alkenyl, the structure is similar to the protoporphyrin as taught by Drummond.

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According to Drummond, tin-protoporphyrins have proved to be innocuous in toxicology studies in animals. Long-term treatment of rats with tin-protoporphyrins resulted in decrease in bilirubin levels (page 90, middle paragraph; page 92, first full paragraph).

Bettelheim in general teaches that amino acids exist as zwitterions and are hence polar. This renders them soluble in water. From this and the teaching of Robinson, one of ordinary skill in the art will recognize that complexing the tin-mesoporphyrins of Robinson with amino acids will enhance the solubility of the porphyrins. Robinson also teaches the use of aqueous solutions of the porphyrins for administration.

Based on the teachings of the prior art above, it would have been obvious to one of ordinary skill in the art at the time the invention was made to make tin mesoporphyrins comprising amino acid residues complexed to the porphyrins, their compositions and use them in a method for treating heme metabolism disorders, hyperbilirubenemia and psoriasis, with a reasonable amount of success since such is seen to be taught in the prior art.

One of ordinary skill in the art would be motivated to make tin mesoporphyrins and use them in a method of treatment as instantly claimed because tin mesoporphyrins, as taught by Drummond, are not toxic and complexing amino acids to the porphyrins would enhance their aqueous solubility.

Even though Drummond teaches protoporphyrins, Robinson's teaching embraces both proto and mesoporphyrins. Proto- and mesoporphyrins are known in the art and are recognized as interchangeable because of their structural similarity. Hence one of ordinary skill in the art would reasonably expect mesoporphyrins as instantly claimed to have the same or substantially similar beneficial therapeutic effects.

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Claims 11-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Niedballa et al (US 5,275,801).

Niedballa et al teach a general method of making a water-soluble porphyrin complex (col. 13, line 34 through col. 14, line 12) wherein a porphyrin core structure of formula (I') (col. 7), comprising amino acid residues is obtained by mixing the core structure (I') with amino acid; complexing with metal ions, which includes tin (col. 13, lines 32-43). Secondary reactions like hydrogenation, esterification, and alkylations are all performed according to literature processes known to one of skill in the art (col. 11, lines 3-7). The use of basic solutions like sodium hydroxide in the steps where amino acids are used in a specific form is taught by Niedballa (col. 14, lines 32-39) as well as the use of metal dichlorides for the introduction of the desired metal (col. 13, line 62). The general method of Niedballa results in a solid or pharmaceutically acceptable liquid. Vacuum drying is used to dry the product (col. 14, lines 16-17).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to mesoporphyrins as instantly claimed by making insignificant changes to the method taught in the prior art. One of ordinary skill in the art would be motivated to do so since the method of Niedballa is a general method applicable to the porphyrin core and gives high yields.

Conclusion

Claims 2-5, 8-31 and 34-37 are rejected.

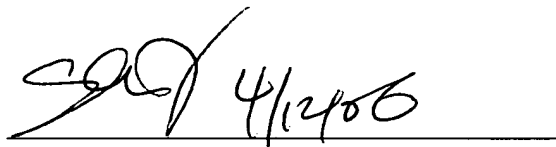
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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathy Krishnan whose telephone number is 571-272-0654. The examiner can normally be reached on 8.30am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

GK

A handwritten signature in black ink, followed by the date "4/12/06". The signature is stylized and appears to be "S. Jiang".

Shaojia A. Jiang
Supervisory Patent Examiner
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